(35% vs. 0, p = 0.001). Neutrophil and platelet recovery was longer in the later cohort, although not statistically significant. Cohort 2 had earlier onset for acute GvHD (64 vs. 49 days, p = 0.048), but late onset for chronic GvHD (202 vs. 122 days, p = 0.001). Although cumulative incidence (CI) of grade II-IV acute GvHD was similar in two cohorts (cohort 1, 62% vs. cohort 2, 53%), there was trend towards decreased grade III-IV acute GvHD (34 vs.16%, p = 0.26) and chronic GvHD (71% vs. 60%, p = 0.08) in cohort 2. At 2-year, CI of relapse, non-relapse mortality, leukemia-free and overall survival were 30%, 30%, 40% and 46%, respectively for all study patients, and no significant differences noted in cohort 1 and 2 for these outcomes. Although a trend towards decreased severe acute GvHD and chronic GvHD is encouraging in the later cohort in this study, more effective novel strategies are required for prevention of GvHD, an issue of major concern in older patients.

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IMMEDIATE ADVERSE EVENTS FOLLOWING INFUSION OF EX VIVO-EXPANDED CORD BLOOD FOR STEM CELL TRANSPLANTATION

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Umbilical cord blood (CB) is utilized with increasing frequency to restore hematopoiesis in bone marrow transplant patients lacking a suitable HLA-matched donor. CB transplantation (CBT) is limited by low cell doses and delays in neutrophil and platelet engraftment. CB progenitors expanded ex vivo prior to transplantation provide more rapid hematopoietic and immune reconstitution, as well as less engraftment failure compared to unmanipulated CB. However, the relative safety regarding the infusion of ex vivo-expanded CB has not been systematically examined. Here we review the immediate adverse events (AE) associated with infusion of ex vivo-expanded CB occurring within 24 hours of infusion in 92 patients enrolled in two clinical CB expansion trials at the MD Anderson Cancer Center from February 2004 to May 2010. The median age of enrolled patients was 42 years (range 3-66), with a predominance of males (n = 60). 47 patients received a CBT for treatment of acute leukemia. 24 patients had a previous stem cell transplant (22 autologous and 2 allogeneic). The majority of patients (n = 80) were pre-medicated prior to transplantation with a combination of diphenhydramine and steroids. All patients received an unmanipulated CB unit followed by infusion of the ex vivo-expanded CB product after 1 hour. ABO mismatching was observed in 28/89 and 22/89 unmanipulated and ex vivo-expanded CB products, respectively. The mean volume of the infusions was 109 mls (range 45-249 mls) for the unmanipulated CB units and 134 mls (range 39-180 mls) for the expanded product. A total of two Grade 1-2 and five Grade 3-4 infusion reactions occurring within 24 hours after CBT of both products were observed. This resulted in an AE rate of 8%. The majority of the AEs manifested as signs of dyspnea and hypoxia and could be attributed to either vasovagal reactions or volume overload. However, no association with patient age, disease, previous transplant, total infusion volume, or ABO incompatibility was observed. In summary, infusion related toxicities in patients who receive an unmanipulated and ex vivo-expanded double CBT appears relatively low. We conclude that infusion of unmanipulated followed by expanded CB products is a safe procedure associated with a low probability of inducing severe reactions. We are currently examining the incidence of infusion related toxicities in patients who have received only unmanipulated CB products.

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PROSPECTIVE TRIAL OF PRE-TRANSPLANT 5-AZACITIDINE ON HEMATOPOIETIC CELL TRANSPLANTATION OUTCOMES FOR MYELODYSPLASTIC SYNDROME AND CMML

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We report the results of a prospective observational clinical trial with the objective of evaluating HCT outcomes following pre-HCT therapy with 5-azacitidine. Twenty-three patients seen in consultation for HCT and medically eligible for a donor search were enrolled and received 5-azacitidine [75mg/m2 for 7 days every 4 weeks] until a suitable donor was identified. Four did not proceed to transplant for the following reasons: failure to obtain insurance approval due to patient age, failure of the pre-HCT organ evaluation although a donor was identified, CNS hemorrhage in setting of chronic anti-coagulation five days prior to HCT admission and one (62 years) declined HCT as only a HLA-A mismatched donor was available. Nineteen patients received a HCT following a myeloablative targeted busulfan fludarabine regimen. Median age at HCT was 57 years (25 – 67). IPSS at diagnosis was Int-1 (2), Int2 (9) and high (5), CMML1 (1), AMLM6 (1) and not evaluable (NE) (1). Cytogenetic risk was good (7), intermediate (5) and poor (7). Three patients had therapy related MDS. Patients received a median of 4 (1-6) cycles of 5-azacitidine. Median time from diagnosis (or time of progression and start of therapy in 2 patients) to HCT infusion was 195 days (107 – 350). Response to 5-azacitidine prior to HCT by the International Working Group 2006 criteria included partial response (8), stable disease (9) and 2 progressed. Two received leukemic induction chemotherapy prior to HCT. IPSS score prior to HCT was Low (1) Int-1 (6), Int2 (9) and poor (1) and CMML1 (2). Source of donor cells was peripheral blood siblings (7), matched unrelated donors (10) and mismatch unrelated donors (2). Median follow-up from HCT is 440 days (83-696). There are 3 patients who did not achieve remission (1) or relapsed (2) and 1 of the three remains alive with active disease. There are 3 non-relapse deaths, 2 due to infection and 1 due to GVHD. All deaths occurred between days 180 – 262. At one year OS is 69% (SE 0.12) and DFS is 63% (SE 0.12). In conclusion, pre-HCT 5-azacitidine was well tolerated, provided control of disease as a bridge to HCT and did not impose additional toxicity after allogeneic HCT with a promising 1 year progression-free survival. Controlled trials are needed to determine whether post-transplant relapse and survival are improved by pre-transplant 5-azacitidine.

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FASTER REGISTRATION ON INTERNATIONAL DONOR REGISTRIES AND SHORTER TIME TO ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION AFTER HAVING FOUND A DONOR CONFERS BETTER OUTCOME IN ACUTE LEUKEMIA PATIENTS

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A patient has 30% chance to find an HLA identical sibling donor (SD) and 40% chance to find a suitable unrelated donor (UD), 40% of registered patients on international registries relapse or die before finding a donor. We evaluated the outcome in acute leukemia (AL) patients, whether they had an HLA identical SD, an UD or no donor (ND) after registration on France Greffe de Moelle (FGM) registry, either transplanted later or not. Secondary objectives were to evaluate the impact of intervals diagnosis-allo-HSCT, donor finding-allo-HSCT, registration-allo-HSCT, on OS and EFS. We analyzed 251 AL patients, 117 (47%) males and 134 females, median age at diagnosis 40 years [16-66], 177 (71%) AML and 75 ALL. Seventy six (30%) patients had an available SD and received allo-HSCT within a median time of 3.5 months (0.5–43) and 38 (15%) had SD but were not transplanted due to early relapse and/or death. For patients with no available SD, a registration on FGM registry was done, 137 patients were registered after a median interval of 2.3 months (0.4-135) from diagnosis, 33 (13%) patients did not find any donor and they received the standard of care; 104 (41%) patients found an UD or UCB unit after a median time of 1.6 months (0.3-26): 86 with UD of which only 60 have been transplanted within a median time of 2.3 months (0.4–14), 18 with UCB of which only 17 were transplanted. Among transplanted patients, 113 (74%) were in CR, 40 in < CR. Fifty (33%) received PBSC, 86 (57%) received BM and 17 (10%) UCB units. For conditioning, 56 (37%) were RIC